Update: Preventing Cervical Cancer with Screening and HPV Vaccination

There are more than 100 strains of Human Papilloma Virus (HPV). About 40 are sexually transmitted, and 14 of those are associated with an increased risk of developing cervical cancer (and other genital cancers in both women and men).[1] Most cases of HPV infection are self-limiting: 90% of women who acquire an HPV infection spontaneously clear it within two years. *Persistent infection with a high-risk strain* of HPV appears to be a necessary but not sufficient condition for the development of cervical cancer. Other risk factors include cigarette smoking, long-term use of oral contraceptives, high parity, and a history of other sexually-transmitted infections.

Cervical cancer was the leading cause of cancer death among women in the United States in the early 1900s. Since Papanicolaou (Pap) cytologic screening became widely available in the 1950s, invasive cervical cancer has become rare in the United States. Cervical cancer has been nearly eliminated among women who are regularly screened.

Transient infection with HPV can lead to ASC-US (abnormal squamous cells of undetermined significance) or LSIL (low-grade squamous intraepithelial lesions) screening results; these cytologic abnormalities typically spontaneously regress as the HPV infection is cleared. Persistent HPV infection with a high-risk strain is associated with an increased risk of developing severe and persistent precancerous cervical lesions.

There are now two vaccines approved for the prevention of HPV infection, quadrivalent (four-strain) Gardasil by Merck, licensed by the FDA in 2006, and bivalent (two-strain) Cervarix by GlaxoSmithKline, licensed in 2009.[2] Both vaccines target the two highest-risk strains of HPV estimated to be associated with 50% to 60% of cases of cervical cancer. Gardasil also targets two strains associated with genital warts. In pre-approval clinical trials and in the few years since they have been used in the general population, both vaccines appear to be moderately to highly effective in preventing infections with the targeted strains of HPV, provided the three-dose course is completed before girls become sexually active and are exposed to HPV. However, both vaccines had an estimated lower limit of efficacy as low as 40% in some of pre-approval clinical trials. The duration of protection against HPV infection is as yet unknown, although a previous recommendation for a booster after the initial three-dose course has been eliminated.

[1] Centers for Disease Control and Prevention, 2007. Human Papilloma Virus: HPV Information for Clinicians. http://www.cdc.gov/std/hpv/common-clinicians/ClinicalBro-fp.pdf

[2] Centers for Disease Control and Prevention, 2010. FDA Licensure of Bivalent Human Papillomavirus Vaccine (HPV2, Cervarix) for Use in Females and Updated HPV Vaccination Recommendations from the Advisory Committee on Immunization Practices (ACIP). MMWR 59:626-629. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5920a4.htm?s_cid=mm5920a4_e

The Advisory Committee on Immunization Practices (ACIP), a national expert panel appointed by the Secretary of the US Department of Health and Human Services, recommends that girls age 11 and 12 years receive three doses of HPV vaccine over the course of six to eight months. Vaccination is approved for girls as young as age 9 years and catch-up vaccination for girls and young women between the ages of 13 and 26 years is approved, provided they have not yet been exposed to HPV. Vaccination is not effective for women with current HPV infections or for women who have previously had and cleared such an infection.

Gardasil was recently licensed by the FDA for use in males age 9 through 26 years to prevent genital warts.[3] Vaccination is not effective if males have or have previously had an HPV infection with the target strains. The ACIP does not recommend routine or universal HPV vaccination for males. Population-based epidemiologic and economic models suggest that increasing coverage among girls to 80% or more is the most effective way to reduce the overall burden of HPV in the population. However, certain subpopulations of males such as men who have sex with men may benefit disproportionately from HPV vaccination.

Regardless of vaccination status, all sexually active women must continue to have Pap screening within three years of becoming sexually active and at regular intervals thereafter because:

- **The approved vaccines target only two of 14 strains of HPV known to increase the risk of cervical cancer.**
- **Nearly half of all cases of cervical cancer are associated with strains of HPV for which there are as yet no vaccines.**
- **The efficacy of the HPV vaccines is generally high but not absolute and there is likely to be individual variation among girls and women in their immunologic response to the vaccine.**
- **The duration of protection conferred by HPV vaccination in childhood is unknown.**
- **Pap screening remains the fundamental protection against cervical cancer for all women, including those who have been vaccinated.**

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[3] Centers for Disease Control and Prevention, 2010. FDA Licensure of Quadrivalent Human Papillomavirus Vaccine (HPV4, Gardasil) for Use in Males and guidance from the Advisory Committee on Immunization Practices (ACIP). MMWR 59:630-632. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5920a5.htm?s_cid=mm5920a5_e